

1-78. (cancelled)

79. (previously presented) A vaccine or inoculum comprising an immunogenic effective amount of immunogenic particles dissolved or dispersed in a pharmaceutically acceptable diluent, wherein said immunogenic particles are comprised of a plurality of recombinant chimeric hepatitis B core (HBc) protein molecules in which said recombinant chimeric HBc protein molecules have a length of up to about 515 amino acid residues that

(a) contain a sequence of at least about 130 of the N-terminal 150 amino acid residues of the HBc molecule that include one or more peptide-bonded heterologous epitopes at the N-terminus, or in the HBc immunogenic loop or a heterologous linker residue for a conjugated epitope present in the HBc immunodominant loop,

(b) contain one to ten cysteine residues toward the C-terminus [C-terminal cysteine residue(s)] of the molecule from the C-terminal residue of the HBc sequence and within about 30 residues from the C-terminus of the chimer molecule,

(c) contain a sequence of at least 5 amino acid residues from HBc position 135 through position 140 toward the HBc C-terminus, and zero to about 100 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus,

said chimer molecules containing no more than about 5 percent conservatively substituted amino acid residues in the HBc sequence as compared to a sequence of SEQ ID NO:246-251 from position 1 through 149, and

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said particles being substantially free of binding to nucleic acids, and being more stable than are particles formed from an otherwise identical HBC chimera that lacks said C-terminal cysteine residue(s) or in which a C-terminal cysteine residue present in the chimera molecule is replaced by another residue, wherein said particle stability is assayed as a measurement of the percentage of full length chimera molecules determined by Coomassie Blue stain of reducing buffer 15%SDS-PAGE results obtained after dilution of purified particles to a concentration of 1 mg/mL in aqueous 50 mM NaPO₄, pH 6.8, with sodium azide added to a final concentration of 0.02% and incubation at 37° C for about 14 days.

80. (previously presented) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBC protein molecules have a length of about 135 to about 515 amino acid residues and contains four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about 71 to about 100 amino acid residues whose sequence includes at least the sequence of the residues of position 5 through position 75 of HBC and optionally includes a heterologous epitope containing up to about 30 amino acid residues peptide-bonded to one of HBC residues 1-4;

(b) Domain II comprises about 5 to about 250 amino acid residues peptide-bonded to HBC residue 75 of Domain I in which (i) at least 4 residues in a sequence of HBC positions 76 through 85 are present peptide-bonded to one to about 245 amino

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acid residues that are heterologous to HBc and constitute a heterologous epitope or a heterologous linker residue for a conjugated epitope;

(c) Domain III is an HBc sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

(d) Domain IV comprises (i) 5 through fourteen residues of a HBc amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, (ii) one to ten cysteine residues [C-terminal cysteine residue(s)] within about 30 residues from the C-terminus of the chimer molecule, and (iii) zero to about 100 amino acid residues in a sequence heterologous to HBc from position 150 to the C-terminus, with the proviso that Domain IV contain at least 6 amino acid residues including said one to ten cysteine residues of (ii), said recombinant chimeric HBc protein molecules being more than are particles formed from an otherwise identical HBc chimer molecule that lacks said C-terminal cysteine residue or in which a C-terminal cysteine residue present in the chimer molecule is replaced by another residue, wherein said particle stability is assayed as a measurement of the percentage of full length chimer molecules determined by Coomassie Blue stain of reducing buffer 15%SDS-PAGE results obtained after dilution of purified particles to a concentration of 1 mg/mL in aqueous 50 mM NaPO₄, pH 6.8, with sodium azide added to a final concentration of 0.02% and incubation at 37° C for about 14 days, and having an amino acid residue sequence in which no more than about 5 percent of the amino acid residues

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are conservatively substituted in the HBC sequence as compared to a sequence of SEQ ID NO:246-251 from position 1 through 149.

81. (original) The vaccine or inoculum according to claim 80 that contains a heterologous linker residue for a conjugated epitope in Domain II and further includes a hapten linked to said heterologous linker residue.

82. (previously presented) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBC protein molecules have a length of about 175 to about 240 amino acid residues and contain four peptide-linked amino acid residue sequence domains from the N-terminus that are denominated Domains I, II, III and IV, wherein

(a) Domain I comprises about the sequence of the residues of position 1 through position 75 of HBC;

(b) Domain II comprises about 5 to about 55 amino acid residues peptide-bonded to HBC residue 75 of Domain I in which at least 4 residues in a sequence of HBC positions 76 through 85 are present peptide-bonded to 6 to about 50 amino acid residues that are heterologous to HBC and constitute a heterologous epitope;

(c) Domain III is an HBC sequence from position 86 through position 135 peptide-bonded to residue 85 of Domain II; and

(d) Domain IV comprises (i) 5 through fourteen residues of a HBC amino acid residue sequence from position 136 through 149 peptide-bonded to the residue of position 135 of Domain III, and (ii) zero to about 50 amino acid residues in a

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sequence heterologous to HBc from position 150 to the C-terminus,

said particles exhibiting a ratio of absorbance at 280 nm to 260 nm of about 1.4 to about 1.6.

83. (original) The vaccine or inoculum according to claim 79 that is adapted for parenteral administration.

84. (original) The vaccine or inoculum according to claim 79 that is adapted for mucosal immunization.

85. (original) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBc protein molecule particles are present in an attenuated strain of *S. typhi*, *S. typhimurium* or a *S. typhimurium*-*E. coli* hybrid.

86. (original) The vaccine or inoculum according to claim 79 wherein said recombinant chimeric HBc protein molecule particles are present in plant tissue.

87. (original) The vaccine or inoculum according to claim 79 that further includes an adjuvant.

88. (original) The vaccine or inoculum according to claim 87 wherein said adjuvant is alum.

89. (original) The vaccine or inoculum according to claim 87 wherein said adjuvant is a small molecule selected from the group consisting of a muramyl dipeptide, 7-substituted-8-

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oxo- or 8-sulfo-guanosine derivative, monophosphoryl lipid A, aluminum or calcium salts.

90. (original) The vaccine or inoculum according to claim 87 wherein said adjuvant is an oil that is emulsified with said immunogenic particles and said pharmaceutically acceptable diluent.

91. (original) The vaccine or inoculum according to claim 90 wherein said emulsion is an water-in-oil emulsion having a water phase and an oil phase.

92. (original) The vaccine or inoculum according to claim 90 wherein said emulsion is an oil-in-water emulsion having a water phase and an oil phase.

93. (original) The vaccine or inoculum according to claim 92 wherein the oil phase of said emulsion comprises squalene.

94. (original) The vaccine or inoculum according to claim 92 wherein the oil phase of said emulsion comprises squalane.

95. (original) The vaccine or inoculum according to claim 90 wherein the water and oil phases of said emulsion are emulsified by an emulsifying agent that is a sorbitan or mannide C₁₂-C₂₄ fatty acid ester.

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96. (original) The vaccine or inoculum according to claim 95 wherein said emulsifying agent is a mannide C₁₂-C₂₄ fatty acid ester.

97. (original) The vaccine or inoculum according to claim 96 wherein said C₁₂-C₂₄ fatty acid of said mannide C₁₂-C₂₄ fatty acid ester is oleic acid.

98-109. (cancelled)

110. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 79, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.

111. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 80, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.

112. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 82, and maintaining that inoculated animal

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for a time period sufficient for that animal to develop an immune response.

113. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 87, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.

114. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 88, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.

115. (original) A method of inducing an immune response in an inoculated host animal that comprises the steps of inoculating a host animal with a vaccine or inoculum according to claim 92, and maintaining that inoculated animal for a time period sufficient for that animal to develop an immune response.